August 7, 1956

Dear Herman:

One of my students, Bob Wright, raised an interesting question about the "four enzymes" mentioned in your discussion.

Where does IV fit into any cycle of Gal utilization? The summation of steps I,II,III is:

ATP + Gal + PGal + URP-PG + URP-PGal — ADP + PGal +PG +URP-PGal +URP-PG

i.e.,

ATP + Gal — ADP + PG (analogous to the hexokinase first step).

The only role I can see for IV is the initial synthesis of catalytic amounts of URP-PG, i.e., a deficiency in IV would show up as a block in the transferase reaction owing to lack of the "coenzyme". Reactions II and III must have equilibria nearly 1.0; I presumably would drive far to the right.

In fact, might it not be possible for an excess of enzyme IV, in the presence of phosphoglucoisomerase and an oxidative or glycolytic sink to so deplete URPPG that step II would be blocked? This may be too fanciful an idea, and I don't want it to distract from the main question, whether "IV" should be presented as part of the galactose cycle, any more, say than the reactions which replenish ATP.

Yours sincerely,

Joshua Lederberg